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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/972,301	11/18/1997	TIMOTHY A. COLEMAN	325800-588(P	5422

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HUMAN GENOME SCIENCES INC
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EXAMINER
KEMMERER, ELIZABETH

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 09/30/2003

33

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	08/972,301	COLEMAN ET AL.	
	Examiner	Art Unit	
	Elizabeth C. Kemmerer, Ph.D.	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 May 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *137-206* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *137-151,204 and 206* is/are allowed.

6)☒ Claim(s) *152-203 and 205* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 24.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *See Continuation Sheet* .

Continuation of Attachment(s) 6). Other: Attachment A, Cert. of Corr. for 6,090,377.

DETAILED ACTION

Status of Application, Amendments, And/Or Claims

Prosecution is hereby re-opened.

The previous indication that all claims were allowable is *withdrawn* in view of the new grounds of rejection set forth below.

Claims 137-206 are under examination.

35 U.S.C. § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 152-203 and 205 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the claimed invention wherein the recited protein comprises SEQ ID NO: 2, does not reasonably provide enablement for the claimed invention reciting variants and fragments of SEQ ID NO: 2. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The claims are directed to isolated protein and compositions comprising the same, wherein the protein is defined as a genus of structures which may vary from SEQ ID NO: 2 by amino acid substitution, insertion and/or deletion. Most of the claims do not require that the recited protein have any biological activity, with the exception of claims

189 and 197, which require that the protein have "at least one biological activity" of amino acids 1 to 168 of SEQ ID NO: 2. The phrase "at least one biological activity" is broadly, reasonably interpreted as reading on trivial activities, such as a nutritional activity, or non-specific immunogenic activity, which virtually all protein and peptides possess.

The specification discloses SEQ ID NO: 2, which is a protein having specific biological activities, including those suggested by the instant specification and U.S. Patent 6,090,377. Although general guidance is provided in the instant specification regarding how to make and screen variants, such does not rise to the level of enabling guidance; rather, it is an invitation for the skilled artisan to experiment by randomly making structural alterations.

As discussed in the previous action on the merits (Paper No. 21, 11 September 2000), the problem of predicting protein structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex. While it is known that many amino acid substitutions are generally possible in any given protein the positions within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of success are limited. Certain positions in the sequence are critical to the protein's structure/function relationship, e.g. such as various sites or regions directly involved in binding, activity and in providing the correct three-dimensional spatial orientation of binding and active sites. These or other regions may also be critical determinants of antigenicity. These regions can tolerate only relatively conservative substitutions or no

substitutions (see Wells, 1990, Biochemistry 29:8509-8517; Ngo et al., 1994, The Protein Folding Problem and Tertiary Structure Prediction, pp. 492-495; both of record). However, Applicant has provided little or no guidance beyond the mere presentation of sequence data to enable one of ordinary skill in the art to determine, without undue experimentation, the positions in the protein which are tolerant to change (e.g. such as by amino acid substitutions or deletions), and the nature and extent of changes that can be made in these positions. Although the specification outlines art-recognized procedures for producing and screening for active muteins, this is not adequate guidance as to the nature of active derivatives that may be constructed, but is merely an invitation to the artisan to use the current invention as a starting point for further experimentation. Even if an active or binding site were identified in the specification, they may not be sufficient, as the ordinary artisan would immediately recognize that an active or binding site must assume the proper three-dimensional configuration to be active, which conformation is dependent upon surrounding residues; therefore substitution of non-essential residues can often destroy activity.

Due to the large quantity of experimentation necessary to determine how to make a useful variant r fragment of SEQ ID NO: 2, the lack of direction/guidance presented in the specification regarding variants and fragments, the absence of working examples directed to same, the complex nature of the invention, the state of the prior art establishing the unpredictability of mutation on overall structure and function, and the breadth of the claims which fail to recite particular biological activities and also embrace

a broad class of structural fragments and variants, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Claims 152-203 and 205 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, whatever *is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116).

With the exception of SEQ ID NO: 2, the skilled artisan cannot envision the detailed chemical structure of the encompassed polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only isolated polypeptides comprising the amino acid sequence set forth in SEQ ID NO: 2, but not the full breadth of the claim meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

35 U.S.C. § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 171, 173-175, 177-179, 181-183, 185, 186, 203, 205 are rejected under 35 U.S.C. 102(b) as being anticipated by Kao et al. (1992, J. Biol. Chem. 267:20239-20247; of record).

Kao et al. teach an isolated protein comprising at least a portion or fragment of SEQ ID NO: 2 or ATCC Deposit No. 97165 (p. 20242, Table 1). This fragment has at least one biological activity of SEQ ID NO: 2 or ATCC Deposit No. 97165, such as nutritional activity or non-specific immunogenic activity. Kao et al. teach the protein

further comprising a heterologous polypeptide (keyhole limpet hemocyanin, p. 20249, left column). The protein is inherently glycosylated. The protein is identical to one that is produced by a cell and then recovered. The protein is disclosed in a composition comprising a pharmaceutically acceptable carrier (the fusion protein used to immunogenize the rabbits at p. 20240 was necessarily such a composition).

Applicant's Request for Interference

Applicant's request for interference with U.S. Patent 6,090,377 under 37 CFR 1.607 in Paper No. 26 (09 March 2001) is noted. Such will not be granted until the instant claims are again in condition for allowance.

Applicant's attention is directed to Attachment A of the instant Office Action, which contains a copy of a Certificate of Correction issued to U.S Patent 6,090,377. The claims of '377 are limited to the full length, 301 amino acid protein of SEQ ID NO: 1 of '377. It is noted that all of the instant claims encompass the full length, 301 amino acid polypeptide claimed in '377. However, neither the claims nor the specification of '377 suggest Applicant's 168 amino acid SEQ ID NO: 2. If claims were presented in the instant application to isolated proteins *consisting of* SEQ ID NO: 2, such would be deemed distinct from the protein claimed in '377.

Conclusion

Claims 137-151, 204 and 206 are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Elizabeth C. Kemmerer, Ph.D. whose telephone number is (703) 308-2673. The examiner can normally be reached on Monday through Thursday, 6:30 a.m. to 4:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne L. Eyler, Ph.D. can be reached on (703) 308-6564. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Elizabeth C. Kemmerer

ECK

ELIZABETH KEMMERER
PRIMARY EXAMINER

ATTACHMENT A

UNITED STATES PATENT AND TRADEMARK OFFICE

CERTIFICATE OF CORRECTION

PATENT NO. : **6,090,377**

DATED : **Jul. 18, 2000**

INVENTOR(S) : **Olga Bandman, Roger Coleman, Janice Au-Young, Lynn E. Murry**

It is certified that error appears in the above-identified patent and that said Letters Patent are hereby corrected as shown below:

Col. 37, lines 32 and 33, delete "at least a portion of".
Col. 37, line 34, delete "at least a".
Col. 38, line 31, delete "portion of".

Signed and Sealed this

Seventeenth Day of April, 2001

Attest:

Nicholas P. Godici

NICHOLAS P. GODICI

Attesting Officer

Acting Director of the United States Patent and Trademark Office